Evolution Insight: Pfizer and BioNtech: a *lightspeed* deal for potential Covid Vaccine.

The Pfizer and BioNTech agreement expands the research and development alliance signed by the companies in 2018 to develop mRNA-based vaccines against influenza.

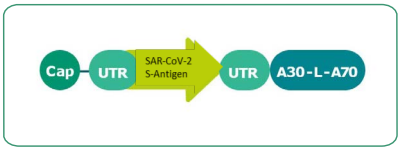
With the latest collaboration, the companies aim to speed-up the development of BioNTech's BNT162 as a potential Covid-19 vaccine via the 'Lightspeed program.'

BioNTech also formed a strategic development and commercialisation partnership with Shanghai Fosun Pharmaceutical to advance BNT162 for protection from Covid-19 in China. As part of the deal, the companies will co-develop the candidate in China and perform clinical trials by utilising Fosun's clinical development, regulatory and commercial expertise in the country.

BioNTech's Covid-19 vaccine

BioNTech's Covid-19-focused project includes four vaccine candidates. Two of these candidates consist of a nucleoside modified mRNA, one includes a uridine containing mRNA and the fourth candidate has self-amplifying mRNA. The company has included a larger spike sequence in two of the vaccine candidates and the spike protein's smaller optimised receptor binding domain (RBD) in the remaining two.

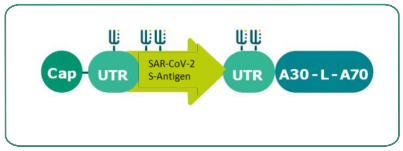
Uridine mRNA (uRNA)[1]



Rationale

- Prime / boost
- Strong adjuvant effect
- Active at low doses
- Strong antibody response
- CD8 T-Cells > CD4 T-Cells

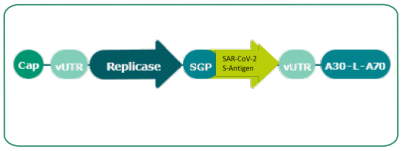
Nucleoside-modified mRNA (modRNA) [2]



Rationale

- Prime/ boost
- Moderate adjuvant effect
- Very strong antibody response
- CD4 T-Cells > CD8 T-Cells

Self-amplifying mRNA (saRNA) [3]



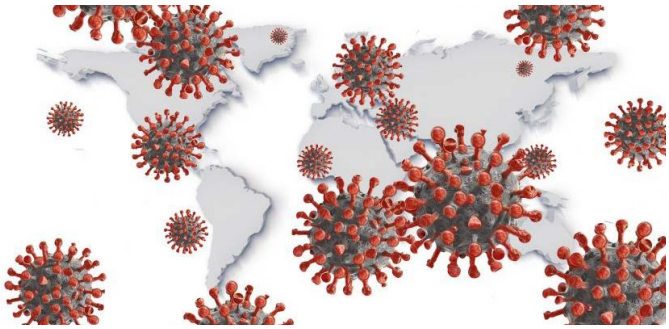
Rationale

- Prime (1x injection)
- Long-term activity
- Very strong antibody response
- Very strong T-Cell response (CD8 and CD4)
- Potent immune protection at low doses (approx. 60x lower dosages required to induce immunity vsuRNA observed in preclinical models)

[1] Kreiter et al., Nature 2015, Kranz, Diken et al., Nature, 2016, Sahin et al., Nature 2017, Reinhard et al., Science 2020
[2] Pardi et al., Nature, 2017, Pardi et al., Mol Ther 2019, [3] Vogel et al., Mol. Ther 2018, Moyo et al., Mol Ther 2019

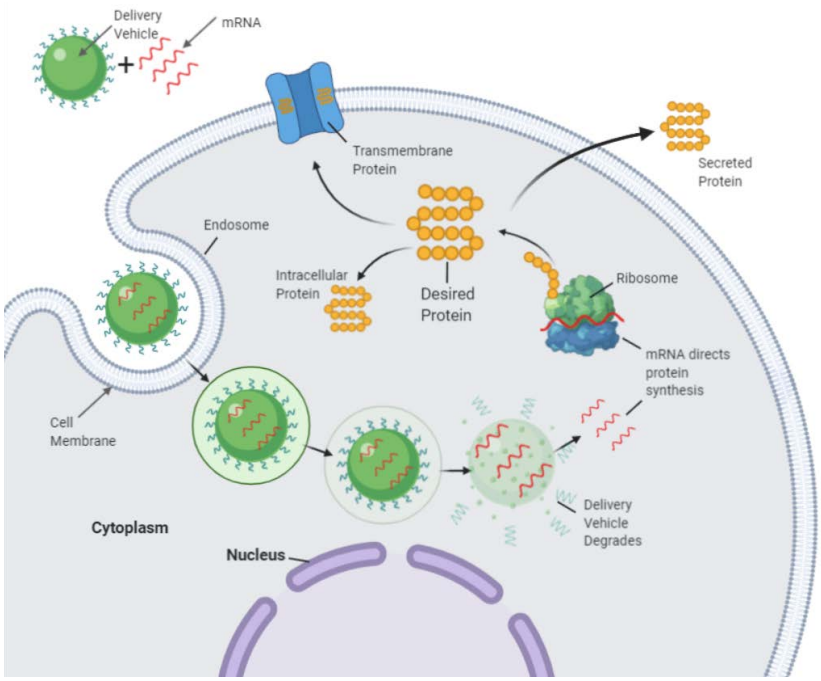
mRNA Pharmaceuticals as Vaccines

Pfizer and BioNTech have begun delivering doses of their coronavirus vaccine candidates for initial human testing in the United States. Trials in Germany have already begun. If successful, Pfizer said it hopes to receive emergency use authorization from the U.S. Food and Drug Administration as early as October. It could distribute up to 20 million doses by the end of 2020, and potentially hundreds of millions next year.



The Use of mRNA Pharmaceuticals as Vaccines

- Synthetic variants of naturally occuring genetic molecules.
- Biochemically defined biopharmaceuticals.
- High purity and free of animal product.
- Inherent immune-activating qualities with no need for additional adjuvant.
- Stimulates both antibody and T-cell immune response at low doses.
- Highly scalable production with potential to manufacture hundreds of millions of doses.



- Mechanism of action of mRNA vaccines: Delivery of mRNA-coded genetic information as blueprint for vaccine into cells of vaccinated individual.
- mRNA uptake into cells results in vaccine antigen synthesis.
- mRNA stimulates immune system of vaccinated individual, generating immune response to the vaccine antigen.

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Scalability

Pfizer plans for raw material manufacturing in St. Louis, drug substance manufacturing in Andover, and formulation and filling is planned to take place at the Kalamazoo site. Additionally, the European site in Puurs, Belgium and BioNtech German facilities will add manufacturing capacity.

Other Scalable Manufacturing COVID -19 Activity

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Pfizer to Outsource Some Drug Production, Focus on Coronavirus Vaccine

The coronavirus pandemic has exposed vulnerabilities across the pharmaceutical industry's global operations. Most of the world's supply of raw chemicals, from which active pharmaceutical ingredients (APIs) are created, originate from Asia. They are then shipped primarily to India or Europe, where the APIs are synthesised. The issue of raw material supply during the pandemic has highlighted the frailty of the pharmaceutical supply chain.

Pfizer is in talks to shift more of its drug (non-COVID 19) production to external partners, as it prepares for large-scale production of its experimental vaccine to prevent COVID-19 - should it prove safe and effective. These external partners are to include Lonza, Thermofisher and Catalent, who will each play a bigger role in producing some of Pfizer's existing medicines. This will allow them to focus production from four of its vaccine manufacturing facilities (including one of its largest U.S. factories) toward the coronavirus vaccine, whilst preventing disruptions in the supply of its other products.

Catalent Lonza ThermoFisher SCIENTIFIC

In addition, BARDA awarded an $812 million (initially $354m) deal to the four year old company; Phlow Corporation, to build a generic medicine and active pharmaceutical ingredients (API) plant in Richmond, Virginia. This comprises part of the administration's push to boost US local drug manufacturing.

References

Kreiter et al., Nature 2015; Kranz, Diken et al., Nature, 2016; Sahin et al., Nature 2017; Reinhard et al., Science 2020
Pardi et al., Nature, 2017; Pardi et al., Mol Ther 2019; Vogel et al., Mol. Ther 2018; Moyo et al., Mol Ther 2019; FierceBiotech; www.epmmagazine.com/